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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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CHOATE, HALL & STEWART LLP
TWO INTERNATIONAL PLACE
BOSTON, MA 02110

EXAMINER	
WILSON, MICHAEL C	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 09/14/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/888,182	KUIDA ET AL.	
	Examiner	Art Unit	
	Michael C. Wilson	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 March 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7 and 12* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7 and 12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 3-14-05 has been entered.

The examiner of this application has changed. Please direct all future correspondence to Examiner Michael C. Wilson, Art Unit 1632.

Claims 8-11 and 13-21 have been canceled. Claims 1-7 and 12 are pending and under consideration in the instant office action.

Drawings

The drawings mentioned throughout the specification cannot be found. If the drawings have not been filed, supplying them in the next response could require a new matter rejection. If the drawings were filed with the original disclosure, please provide the drawings along with proof that the drawings were filed with the original disclosure.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-7 and 12 are rejected under 35 U.S.C. 101 because the claimed invention lacks patentable utility.

REVISED INTERIM UTILITY GUIDELINES TRAINING MATERIALS repeated

from http://www.uspto.gov/web/menu/utility.pdf

"Specific Utility" - A utility that is specific to the subject matter claimed. This contrasts with a general utility that would be applicable to the broad class of the invention. For example, a claim to a polynucleotide whose use is disclosed simply as a "gene probe" or "chromosome marker" would not be considered to be specific in the absence of a disclosure of a specific DNA target. Similarly, a general statement of diagnostic utility, such as diagnosing an unspecified disease, would ordinarily be insufficient absent a disclosure of what condition can be diagnosed.

"Substantial utility" - a utility that defines a "real world" use. Utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utilities. For example, both a therapeutic method of treating a known or newly discovered disease and an assay method for identifying compounds that themselves have a "substantial utility" define a "real world" context of use. An assay that measures the presence of a material, which has a stated correlation to a predisposition to the onset of a particular disease condition, would also define a "real world" context of use in identifying potential candidates for preventive measures or further monitoring. On the other hand, the following are examples of situations that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use and, therefore, do not define "substantial utilities":

A. Basic research such as studying the properties of the claimed product itself or the mechanisms in which the material is involved.

B. A method of treating an unspecified disease or condition. (Note, this is in contrast to the general rule that treatments of specific diseases or conditions meet the criteria of 35 U.S.C. 101.)

C. A Method of assaying for or identifying a material that itself has no "specific and/or substantial utility".

D. A method of making a material that itself has no specific, substantial, and credible utility.

E. A claim to an intermediate product for use in making a final product that has no specific, substantial, and credible utility.

(Page 5-7 of utility guidelines).

> A "well-known utility" is a specific, substantial and credible utility which is well know, immediately apparent, or implied by the specification's disclosure of the properties of the material, alone or taken with the knowledge of one skilled in the art. Neither a "well-established utility" nor a "specific utility" applies to any utility that one can dream up for an invention or a utility that would apply to virtually every member of a general class of materials, such as proteins or DNA.
>
> (Paragraph bridging pg 32-33 of utility guidelines).

Claim 1 is drawn to a transgenic mouse whose genome is heterozygous for a mutation engineered into the Erk5 gene, wherein in a homozygous state said mutation results in a functionally deficient Erk5 gene, failure to produce a functional Erk5 protein, and embryonic death characterized by a lack of vasculogenesis and angiogenesis, and wherein interbreeding of said mouse results in at least some homozygous embryos that fail to produce a functional Erk5 gene and undergo embryonic death.

Claim 3 is drawn to a mouse embryo whose genome is homozygous for a mutation engineered into the Erk5 gene, wherein the mutation results in a functionally deficient Erk5 gene, failure to produce a functional Erk5 protein, and embryonic death characterized by a lack of vasculogenesis and angiogenesis.

Claim 6 is drawn to a chimeric mouse which comprises cells that heterozygous for a mutation engineered into the Erk5 gene, wherein in a homozygous state said mutation results in an embryo characterized by a functionally deficient Erk5 gene, failure to produce a functional Erk5 protein, and a lack of vasculogenesis and angiogenesis and a failure to survive to birth and wherein interbreeding of said chimeric mouse results in at least some heterozygous for a mutation engineered into the Erk5 gene, wherein interbreeding of said heterozygous offspring results in at least some homozygous

embryos that fail to produce a functional Erk5 gene and undergo embryonic death characterized by a lack of vasculogenesis and angiogenesis.

The specification teaches making Erk5 knockout mice (pg 21). Heterozygous mice were normal (pg 22, line 29). Breeding heterozygous mice did not produce any viable offspring (pg 22, lines 29-31). The yolk sac of homozygous embryos was determined to lack vasculature (pg 23, lines 18-21).

The only disclosed use for the heterozygous mouse is to make the homozygous mouse. However, the homozygous mouse does not have a specific or substantial utility. The specification describes using the homozygous mouse in various assays to determine why the mice died in utero. This is not a substantial utility because it does not reveal the function of the Erk5 gene. While applicants determined homozygous mice failed to have normal vasculogenesis or angiogenesis (pg 24-25), applicants did not reveal the role of Erk5 in vasculogenesis or angiogenesis. Without such guidance, using the homozygous mouse embryos to evaluate the lack of vasculogenesis or angiogenesis does not have a substantial utility.

Applicants used wild-type mice in expression analysis (pg 25-27); applicants did not use knockout mice or cells with a knockout. If the knockout mice were used for expression analysis, merely determining where the Erk5 gene is expressed is not substantial because it does not reveal the function of the Erk5 gene in vasculogenesis or angiogenesis.

The knockout mice made by applicants are not models of disease. The specification does not teach any diseases in humans linked to a disruption in the Erk5

gene or identify any compounds capable of treating a disease using the mice. Without such guidance, the mice are not models of disease.

Knockout -/- or -/+ Erk5 mice did not have a "well-known utility" to reveal the function of Erk5. It was well known at the time of filing that knockout mice existed and were used for scientific research. However, scientific research is not the same as "patentable utility" or a "well-established" utility because the mouse may never reveal the function of the knocked out gene. The knockout mice claimed provide a clue that Erk5 is involved in the pathway of vasculogenesis and angiogenesis; however, merely revealing the pathways in which a gene is involved is insubstantial unless the role of the gene within the pathways is revealed. Using mice merely to obtain reveal a pathway in which the gene is involved is not a "substantial utility." Significant further research would have been required to determine the function of the Erk5 gene within the developmental pathway and may not require the knockout mouse claimed. In other words, the function of the Erk5 gene may never be determined from the knockout mouse. "Further research" is specifically mentioned in the utility guidelines:

> [T]he following are examples of situations that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use and, therefore, do not define "substantial utilities":
>
> A. Basic research such as studying the properties of the claimed product itself or the mechanisms in which the material is involved.

Even applicants own further research did not reveal the function of the Erk5 gene. Thus, using the mouse claimed to reveal the function of a gene is not a substantial utility because it may never reveal the function of the gene and because further research would be required to do so.

The mice claimed do not correlate to gas chromatographs, screening assays and nucleotide sequencing methods. Gas chromatographs, screening assays and sequencing have specific, credible and substantial utilities. Gas chromatographs separate the chemical components of a compound and identify them. Screening assays have various functions, but may be used, for example, to determine the amount of protein expression in a population of cells. Sequencing methods provide the nucleotide sequence of a nucleic acid molecule. Unlike gas chromatographs, screening assays or sequencing methods, the mice claimed are capable of providing data, but the data may not reveal the function of the gene or provide any substantially useful information. Applicant provides evidence by showing the mice claimed were used in analyses without determining the function of the Erk5 gene. Further research would be required to determine the function of Erk5 using the knockout mice described in the specification. The utility guidelines state using a product for further research is not a "substantial" utility. In this case, the analyses only provide a clue that the Erk5 gene is involved in vasculogenesis and angiogenesis. Therefore, using the mouse claimed as a research tool, specifically for further analyses, does not provide any substantial utility.

Using the mouse claimed to reveal that Erk5 is involved in a vasculogenesis and angiogenesis pathway lacks a specific utility because it does not reveal the specific role of Erk5 in the vasculogenesis or angiogenesis pathway.

Claim 2, directed toward a cell isolated from the heterozygous transgenic mouse of claim 1, lacks utility. The specification does not describe any use for a cell isolated

from a heterozygous mouse. The specification describes analyzing tissues isolated from homozygous mice but not heterozygous mice. If the cells of claim 2 are merely used for phenotype analyses, the cells do not have a substantial use for reasons above.

Likewise, claim 4, directed toward a cell isolated from the homozygous mouse of claim 2, lacks utility because merely using the cells for phenotype analyses does not have a substantial utility for reasons above.

Claims 5 and 12, directed toward an isolated mouse cell heterozygous for the Erk5 disruption, lack utility. The specification does not describe any use for an isolated mouse cell heterozygous for the Erk5 disruption. The specification describes analyzing tissues isolated from homozygous mice but not heterozygous mice. If the cells of claims 5 and 12 are used for making the transgenic mouse heterozygous for the Erk5 disruption, the cells do not have a specific or substantial utility because the mice do not have a specific or substantial utility for reasons above.

Claim 7, directed toward a cell isolated from the chimeric mouse heterozygous for the Erk5 disruption, lacks utility for reasons in the paragraphs above.

Enablement

Claims 1-7 and 12 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific or substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

In summary, homozygous mice that die in utero do not have an enabled use because they are dead and do not reveal the function of the Erk5 gene in vasculogenesis or angiogenesis. Heterozygous mice used to make homozygous mice are not enabled because the homozygous mice do not have an enabled use. The cells of claims 2, 4, 5, 7 and 12 do not have an enabled use because using the cells to make the knockout mice that do not have an enabled use is not an enabled use and because using the cells in phenotypic analyses without determining the role of Erk5 in vasculogenesis and angiogenesis is not an enabled use.

Written description

The written description rejection regarding species other than mice has been withdrawn because the claims are limited to mice, cells isolated from mice or mouse cells.

New matter

Claims 1-7 and 12 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The written description rejection regarding species other than mice has been withdrawn because the claims are limited to mice, cells isolated from mice or mouse cells.

The limitation of "failure to produce functional Erk5 protein" as newly amended in claims 1, 3, 6 is new matter. Failure to produce functional Erk5 protein is not the same as "a functionally deficient Erk5 gene" in original claim 3. A functionally deficient gene may produce a functionally deficient protein, which is not the same as a one that fails to produce functional protein.

The limitation of "failure to produce functional Erk5 gene" as newly amended in claim 1 is new matter for the same reasons.

The limitation of "lack of expression of mRNA encoding functional Erk5 protein from the gene in said cell" in claims 2 and 5 is new matter. Nowhere does the specification teach the cells isolated from heterozygous mice lack Erk5 mRNA expression.

The limitation of "wherein said mutation results in failure to transcribe an mRNA encoding a functional Erk5 protein from the gene in said cell" in claim 7 is new matter for the same reasons.

Conclusion

The claims remain free of the prior art of record because the prior art of record did not teach i) a transgenic mouse whose genome is heterozygous for a mutation engineered into the Erk5 gene as claimed, wherein in a homozygous state said mutation results in a functionally deficient Erk5 gene, failure to produce a functional Erk5 protein, and embryonic death characterized by a lack of vasculogenesis and angiogenesis, and wherein interbreeding of said mouse results in at least some homozygous embryos that fail to produce a functional Erk5 gene and undergo

embryonic death; ii) a mouse embryo whose genome is homozygous for a mutation engineered into the Erk5 gene, wherein the mutation results in a functionally deficient Erk5 gene, failure to produce a functional Erk5 protein, and embryonic death characterized by a lack of vasculogenesis and angiogenesis; iii) an isolate mouse cell heterozygous for a mutation engineered into the Erk5 gene and lack of expression of mRNA encoding functional Erk5 protein from the gene in said cell, wherein said mutation results in embryonic death characterized by a lack of vasculogenesis and angiogenesis when present in an embryo homozygous for said mutation; or iv) a chimeric mouse which comprises cells that heterozygous for a mutation engineered into the Erk5 gene, wherein in a homozygous state said mutation results in an embryo characterized by a functionally deficient Erk5 gene, failure to produce a functional Erk5 protein, and a lack of vasculogenesis and angiogenesis and a failure to survive to birth and wherein interbreeding of said chimeric mouse results in at least some heterozygous for a mutation engineered into the Erk5 gene, wherein interbreeding of said heterozygous offspring results in at least some homozygous embryos that fail to produce a functional Erk5 gene and undergo embryonic death characterized by a lack of vasculogenesis and angiogenesis.

No claim is allowed.

Inquiry concerning this communication or earlier communications from the examiner should be directed to Michael C. Wilson who can normally be reached at the office on Monday, Tuesday, Thursday and Friday from 9:30 am to 6:00 pm at 571-272-0738.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

If attempts to reach the examiner are unsuccessful, the examiner's supervisor, Ram Shukla, can be reached on 571-272-0735.

The official fax number for this Group is (571) 273-8300.

Michael C. Wilson

MICHAEL WILSON
PRIMARY EXAMINER